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Impact of Myocardial Salvage Assessed by ^{99m}Tc-Sestamibi Scintigraphy on Cardiac Autonomic Function in Patients Undergoing Mechanical Reperfusion Therapy for Acute Myocardial Infarction

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OBJECTIVES The purpose of this study was to analyze the impact of myocardial salvage on cardiac autonomic function in patients undergoing mechanical reperfusion therapy for acute myocardial infarction (MI).

BACKGROUND Heart rate deceleration capacity (DC) and heart rate turbulence slope (TS) are strong predictors of post-MI mortality. Salvage of jeopardized myocardium is the main mechanism by which patients benefit from reperfusion therapy. The impact of myocardial salvage on DC and TS is unknown.

METHODS The study enrolled 854 consecutive patients undergoing mechanical reperfusion therapy for first MI. Paired ^{99m}Tc-sestamibi scintigraphy studies (acute and 7 to 14 days after reperfusion) were used to calculate myocardial salvage index. DC and TS were assessed from Holter recordings 7 to 14 days after reperfusion. Patients were categorized into 3 groups by salvage index: $<$30% (n = 244), 30% to 60% (n = 257), and $\geq$60% (n = 353).

RESULTS In the 3 groups, DC was 5.2 (interquartile range 3.5 to 7.1) ms, 5.7 (4.1 to 7.3) ms, and 6.4 (5.0 to 8.0) ms, whereas TS was 5.3 (2.6 to 8.4) ms/R-R interval, 6.9 (3.2 to 11.7) ms/R-R interval, and 7.8 (4.1 to 13.2) ms/R-R interval, respectively ($p < 0.0001$ for both). After adjustment for left ventricular ejection fraction (LVEF), initial perfusion defect, creatine kinase, age, diabetes mellitus, sex, and medical therapy, patients with salvage index $<$30% had a 2.6-fold risk (95% confidence interval: 1.8 to 3.9, $p < 0.001$) of having abnormal DC ($\leq$4.5 ms) or TS ($\leq$2.5 ms/R-R interval) compared with patients with salvage index $\geq$60%. However, patients who had autonomic dysfunction defined by abnormal DC and TS had a poor prognosis independent of whether or not the salvage index was $<$30% (5-year mortality rates of 16.5% and 17.3%, respectively). In contrast, prognosis was excellent when both factors were normal (5-year mortality rates of 2.9% and 4.0%, respectively). Predictive value of impaired LVEF ($\leq$40%) was also independent of salvage index. Multivariably, both autonomic dysfunction and impaired LVEF were independent predictors of 5-year mortality.

CONCLUSIONS In patients undergoing mechanical reperfusion therapy for acute MI, salvage index is an independent predictor of autonomic dysfunction but does not affect its prognostic value. (J Am Coll Cardiol Img 2009;2:449–57) © 2009 by the American College of Cardiology Foundation

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Myocardial infarction (MI) leads to cardiac autonomic dysfunction in a considerable number of patients (1). There is a large body of experimental and clinical evidence that post-MI autonomic dysfunction is associated not only with increased susceptibility to malignant tachyarrhythmias but also with increased mortality risk. Consequently, markers of autonomic dysfunction such as depressed heart rate variability (HRV) or impaired baroreflex sensitivity have been proposed for post-MI risk stratification (2–4). Many factors have been identified to affect autonomic function after MI. These include age, sex, previous MIs, presence or absence of diabetes mellitus, and therapeutic interventions (3).

In contrast, little is known about the autonomic impact of reperfusion therapy after MI. The aim of post-MI reperfusion strategy is restoration of epicardial blood flow in the occluded artery, leading to salvage of the jeopardized myocardium and preservation of left ventricular (LV) pump function. The ability of reperfusion to salvage myocardium depends not only on complete and sustained restoration of epicardial flow but also on the degree of restoration of myocardial perfusion, which can be reliably quantified by ^{99m}Tc-sestamibi imaging. The difference between perfusion defects measured before and several days after reperfusion therapy characterizes the extent of salvaged myocardium (5–8). In several studies, this myocardial salvage has been shown to be associated with outcome after MI and has subsequently been used as a surrogate measure of mortality in randomized trials (9). While restoration of epicardial blood flow in the infarct artery was shown to correlate with a less severe impairment of autonomic function (4,10), no data exist in respect of the impact of myocardial salvage on autonomic function.

We therefore aimed at assessing the relationship between myocardial salvage and cardiac autonomic function in patients undergoing reperfusion therapy for acute MI. To characterize the cardiac autonomic status, we employed 2 novel autonomic markers, namely, deceleration capacity (DC) and heart rate turbulence (HRT). These autonomic markers have previously been validated in independent patient populations as strong predictors of post-MI mortality (11–15).

ABBREVIATIONS AND ACRONYMS

DC = deceleration capacity
HRT = heart rate turbulence
HRV = heart rate variability
MI = myocardial infarction
LV = left ventricular
LVEF = left ventricular ejection fraction
SDNN = standard deviation of all normal-to-normal intervals
TS = turbulence slope
VPC = ventricular premature complex

METHODS

Study population. Patients were recruited at the 1.Medizinische Klinik rechts der Isar and the Deutsches Herzzentrum Munich, Germany. Consecutive patients presenting with acute MI between 1996 and 2003 were enrolled in a prospective database. In this study, patients were only included if they were ≤75 years of age, presented with sinus rhythm, and underwent primary mechanical reperfusion therapy for MI. Patients <18 years, with known or suspected pregnancy, or with history of previous MI were excluded. MI was diagnosed in the presence of at least 2 of the following criteria: chest pain for ≥20 min, creatine kinase-myocardial band above the twice upper normal limit, and/or ST-segment elevation of ≥0.1 mV in 2 or more limb leads or ≥0.2 mV in 2 or more contiguous precordial leads at hospital admission. Diabetes mellitus was considered present if the patient was receiving treatment (diet, tablets, or insulin). Patients were followed up for a median of 4.1 (2.5 to 5.0) years. All investigations were performed for clinical reasons; the local ethics committee approved the data registry collection.

Mechanical reperfusion therapy. Immediately after admission to the intensive care unit, all patients received 500 mg ticlopidine or 600 mg clopidogrel orally, a bolus of 500 mg aspirin, and 60 U/kg unfractionated heparin (to a maximum dose of 5,000 U) intravenously. Thereafter, coronary angiography and percutaneous coronary intervention (PCI) were performed at the catheterization laboratory.

Left ventricular ejection fraction. In all patients, left ventricular ejection fraction (LVEF) was assessed by LV angiography or biplane echocardiography during the second week after the index infarction. Left ventriculography was performed in single-plane, 30° right anterior oblique projection technique using a digital angiographic system (Hicor, Siemens, Erlangen, Germany). The LVEF was calculated by the area-length method. In 266 patients, LVEF was assessed by single-plane echocardiography using a phased-array system (Sonos 5500, Philips, Andover, Massachusetts). Calculation of LVEF was based on a modified Simpson rule algorithm in the apical 4-chamber view.

Radionuclide studies. Before the start of reperfusion therapy, all patients received an intravenous injection of 1,000 MBq (27 mCi) of ^{99m}Tc-sestamibi. Single-photon emission computed tomography was performed 6 to 8 h afterward. Follow-up ^{99m}Tc-sestamibi imaging was performed 7 to 14 days after

reperfusion therapy using the same procedure as at the initial assessment. The methods of radionuclide studies were described elsewhere (7,8). The following 3 parameters were calculated: initial perfusion defect and final infarct size (perfusion defect at follow-up studies), both expressed as a percentage of left ventriclular myocardium; and salvage index, that is, the proportion of the initial perfusion defect that recovered after reperfusion therapy (7,8). Patients were categorized into 3 different prospectively defined groups according to salvage index: <30% (group 1), 30% to 60% (group 2), and ≥60% (group 3).

Assessment of autonomic markers. Full 24-h Holter recordings were made within the second week after index MI. The recordings were routinely processed using standard commercial equipment (Oxford Excel Holter System, Oxford Instruments, Abingdon, United Kingdom; Pathfinder 700, Reynolds Medical, Hertford, United Kingdom; or Mortara Holter System, Mortara Instrument, Milwaukee, Wisconsin) to obtain sequences of individual R-R intervals together with morphological QRS classifications. Using these sequences, DC and HRT slope (TS) were calculated as previously described (11,15,16). The DC and TS were dichotomized at established cutoff values of 4.5 ms and 2.5 ms/R-R interval, respectively (11,15,16). If a patient had no ventricular premature complexes (VPC) suitable for HRT calculation but was otherwise in sinus rhythm, TS was classified as normal (12,17).

As proposed by the Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology (3), the following conventional HRV measures were calculated from the 24-h Holter recordings: standard deviation of all normal-to-normal intervals (SDNN), standard deviation of the averages of normal-to-normal interval calculated over 5-min periods, and square root of the mean of the sum of squared differences between adjacent normal-to-normal intervals. Spectral HRV components were also calculated using fast Fourier transformation distinguishing ultra low (<0.0033 Hz), very low (0.0033 to 0.04 HZ), low (0.04 to 0.15 Hz), and high (0.15 to 0.40 Hz) frequency components.

Statistical analysis. Continuous variables are presented as median and interquartile range (IQR). Qualitative data are expressed as percentages. Continuous variables were compared by the Kruskal-Wallis test. Qualitative data were compared by the chi-square test. Binary logistic regression analysis was used to test the independency of the relationship between myocardial salvage and autonomic dysfunction from infarction characteristics, clinical covariates, and treatment (initial perfusion defect, LVEF, maximum level of creatine kinase, age ≥65 years, presence of diabetes mellitus, sex, treatment with aspirin, beta-blockers, angiotensin-converting enzyme inhibitors, and statins). For this analysis, the initial perfusion defect, maximum level of creatine kinase, and LVEF were dichotomized at their median. Survival curves were estimated by the Kaplan-Meier method (18) and compared using the 2-sided log-rank test (19). The influence of autonomic dysfunction and LVEF on mortality was estimated with the Cox proportional hazards model adjusted for salvage index category. The relationship between initial perfusion defect, final infarction size, and the outcome of autonomic markers was also visualized. Differences were considered statistically significant if $p < 0.05$ (version 11.0, SPSS Inc., Chicago, Illinois).

RESULTS

Between 1996 and 2003, paired sestamibi studies and Holter recordings were available for 1,005 consecutive patients. Of these, 48 patients were excluded because they did not undergo primary PCI (thrombolytic therapy in 35 patients, coronary artery bypass grafting in 6 patients, no reperfusion therapy in 7 patients). Of the remaining 957 patients, 103 patients were excluded because they had previous infarctions. Thus, the population of this study consisted of 854 patients who underwent primary PCI for their first MI. During follow-up of 5 years, 40 patients died. Characteristics of the study population are shown in the left column of Table 1. Median initial perfusion defect was 25% of the left ventricle (IQR 15% to 43%), and median final infarct size was 10% of the left ventricle (IQR 4% to 23%). Median salvage index was 50.0% (IQR 25.0% to 76.5%).

Figure 1 shows the impact of initial perfusion defect and final infarct size on DC and TS. Both initial perfusion defect and final infarct size had an obvious impact on DC and TS, with larger defects associated with more abnormal values.

Of the study population, 244, 257, and 353 patients had salvage index <30% (group 1), 30% to 60% (group 2), and ≥60% (group 3), respectively. Baseline characteristics of the 3 groups are shown in Table 1. Patients with low salvage index had lower LVEF and higher values of peak creatine kinase, and were more often prescribed diuretics. Moreover, in patients with low salvage index, the interval between onset of pain to hospital admission was longer, and TIMI (Thrombolysis In Myocardial

Table 1. Baseline Characteristics of Study Population and 3 Salvage Index Groups

Characteristic	All Patients	Salvage Index <30% (Group 1)	Salvage Index 30% to 60% (Group 2)	Salvage Index ≥60% (Group 3)	p Value*
n	854	244	257	353	—
Age, yrs	58 (50–65)	59 (51–65)	57 (50–64)	58 (50–66)	0.64
Female, %	17	16	14	19	0.26
Diabetes mellitus, %	17	14	18	17	0.52
Peak creatine kinase, U/l	1,584 (802–2,775)	2,416 (1,016–3,979)	1,888 (939–3,110)	1,104 (642–1,882)	< 0.001
Time-to-admission interval, h	6.8 (2.8–12.3)	8.5 (3.3–13.8)	5.8 (2.5–11.0)	6.5 (2.5–13.3)	0.02
Door-to-balloon interval, h	1.1 (0.7–1.8)	1.2 (0.8–2.0)	1.1 (0.8–1.8)	1.1 (0.7–1.8)	0.84
TIMI III after PCI, %	88.5	84.4	82.3	95.4	< 0.001
Infarct-related artery, %					
LAD	43.8	41.4	37.4	50.1	
RCA	46.7	49.2	53.3	40.2	0.02
LCx	9.5	9.4	9.3	9.6	
Multivessel disease	59.0	63.1	58.8	56.4	0.26
LVEF, %	54 (46–62)	49 (40–57)	52 (45–60)	59 (51–65)	< 0.001
Aspirin, %	98	97	98	98	0.60
Beta-blocker, %	96	95	96	97	0.52
ACE inhibitors, %	95	95	95	94	0.95
Statins, %	93	93	93	93	0.96
Diuretics, %	39	49	42	30	< 0.001

*The p value for comparisons among the 3 groups. Continuous variables are shown as median (interquartile range).
ACE = angiotensin-converting enzyme; LAD = left anterior descending artery; LCx = circumflex artery; LVEF = left ventricular ejection fraction; PCI = percutaneous coronary intervention; RCA = right coronary artery; TIMI = Thrombolysis In Myocardial Infarction.

Infarction) flow grade 3 was less often achieved. No differences were observed for age, sex, and presence of diabetes mellitus.

Figure 2 shows the distribution of DC and TS in the 3 salvage index groups. Both DC and TS differed significantly in the groups (both $p < 0.0001$) (Table 2). Differences between these groups were also found for conventional HRV measures (Table 2).

Abnormal values of either DC or TS were found in 279 (32.7%) patients. Of these, 250 (29.3%) had

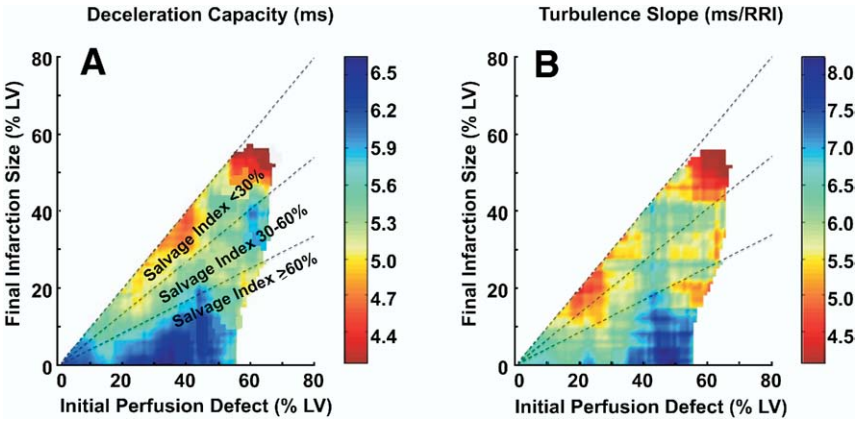

Figure 1. Heat Maps

The so-called "heat maps" showing the level of expression of deceleration capacity **(A)** and turbulence slope **(B)** for combinations of initial perfusion defect (x-axis) and final infarct size (y-axis). The level of expression of the autonomic variable is indicated by color (**blue** indicates more normal values, and **red** indicates more abnormal values). **Dashed lines** show combinations of initial perfusion defect and final infarct size resulting in salvage indices of 0%, 30%, and 60%, respectively. Sliding window technique was used to create the maps. Window size of 10% × 10% was used (i.e., combinations within this range were considered comparable), and the median value of the autonomic markers is shown for the different combinations (combinations with <20 observations were excluded). LV = left ventricle.

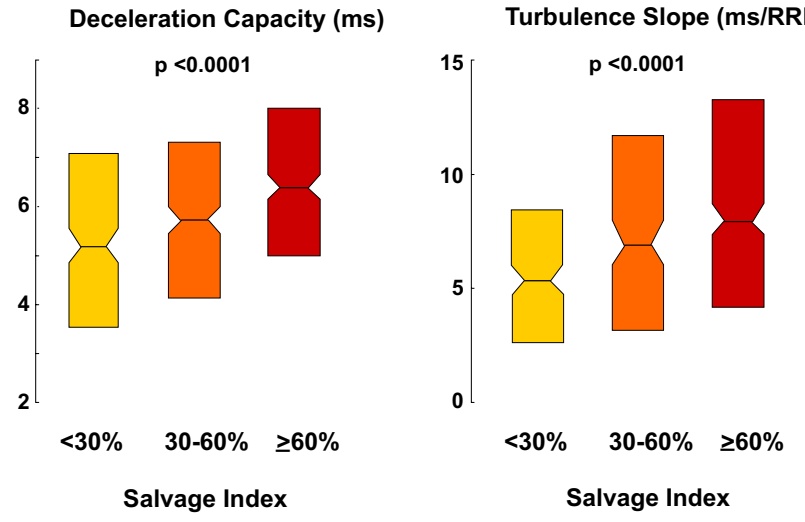

Figure 2. Influence of Myocardial Salvage on Markers of Autonomic Function

Deceleration capacity and turbulence slope in patients with low (<30%), medium (30% to 60%), and high (≥60%) salvage index.

abnormal DC and 97 (11.4%) had abnormal TS. Table 3 shows univariate and multivariate logistic regression analysis for prediction of abnormal DC or TS. Univariately and multivariately, salvage index ≤30% was a highly significant predictor of abnormal DC or abnormal TS, with relative risks (RR) of 2.9 (95% CI: 2.1 to 4.1) and 2.6 (95% CI: 1.8 to 3.9), respectively ($p < 0.001$ for both). Accordingly, salvage index had significant impact on the prevalence of autonomic dysfunction (Fig. 3).

However, as shown in Figure 4 (upper panels), salvage index had no direct impact on prognostic value of autonomic dysfunction. When autonomic dysfunction was present, it indicated poor prognosis irrespective of the amount of salvaged myocardium. Thus, patients with autonomic dysfunction (DC and TS abnormal) had 5-year mortality rates of 16.5% and 17.3% when salvage index was <30% and ≥30%, respectively (Fig. 4). In contrast, prognosis was excellent when both factors were normal (5-year mortality rates of 2.9% and 4.0% in patients with salvage index <30% and ≥30%, respectively). Similar figures were observed when patients were stratified according to presence or absence of LV dysfunction (Fig. 4, lower panels): salvage index substantially influenced prevalence of LV dysfunction (37.1% vs. 9.7% of patients with salvage index <30% and ≥30%, respectively). However, when LV dysfunction was present, prognosis was poor. This was substantiated by multivariable analysis in which both autonomic dysfunction and LVEF ≤40% were independent predictors of 5-year mortality whereas salvage index was not (Table 4).

Table 2. Deceleration Capacity, Heart Rate Turbulence, and Heart Rate Variability in Study Population and 3 Salvage Index Groups

Variable	All Patients	Salvage Index			p Value
		<30%	30% to 60%	≥60%	
DC, ms	5.9 (4.2–7.6)	5.2 (3.5–7.1)	5.7 (4.1–7.3)	6.4 (5.0–8.0)	< 0.001
TS, ms/R-R interval*	6.5 (3.3–11.2)	5.3 (2.6–8.4)	6.9 (3.2–11.7)	7.8 (4.1–13.2)	< 0.001
SDNN, ms	96 (76–120)	87 (69–109)	94 (77–119)	104 (82–127)	< 0.001
SDANN, ms	68 (54–88)	63 (49–80)	66 (54–90)	74 (57–90)	< 0.001
RMSSD, ms	26 (18–34)	23 (17–32)	26 (18–34)	27 (20–35)	< 0.001
ULF, ms^2	5,686 (3,437–8,935)	4,956 (2,648–8,058)	5,511 (3,699–9,183)	6,312 (3,925–10,031)	< 0.001
VLF, ms^2	1,196 (666–2,090)	939 (527–1,826)	1,152 (662–1,984)	1,419 (850–2,353)	< 0.001
LF, ms^2	306 (153–589)	250 (111–535)	273 (149–546)	382 (211–693)	< 0.001
HF, ms^2	94 (47–182)	77 (36–150)	88 (47–188)	111 (57–194)	< 0.001

Variables are shown as median (interquartile range). *Turbulence slope (TS) could only be assessed in 600 of 854 patients because of missing ventricular premature complexes.
DC = deceleration capacity; HF = high frequency; LF = low frequency; RMSSD = square root of the mean of the sum of squared differences between adjacent normal-to-normal (NN) intervals; SDANN =standard deviation of the average NN interval calculated over 5-min segments; SDNN = standard deviation of all NN intervals; TO = turbulence onset; ULF = ultra-low frequency; VLF = very low frequency.

Table 3. Univariate and Multivariate Logistic Regression Analysis for Prediction of Abnormal Deceleration Capacity or Abnormal Turbulence Slope

	Univariate Analysis		Multivariate Analysis	
Variable	**Relative Risk**	**p Value**	**Relative Risk**	**p Value**
Salvage index, %				
30–60	2.1 (1.5–3.0)	< 0.001	2.0 (1.4–3.0)	< 0.001
≤30	2.9 (2.1–4.1)	< 0.001	2.6 (1.8–3.9)	< 0.001
Initial perfusion defect >25%*	1.7 (1.3–2.3)	< 0.0001	1.3 (0.9–1.9)	0.10
Peak creatine kinase >1,584 U/l*	1.8 (1.3–2.4)	< 0.0001	0.8 (0.5–3.0)	0.36
LVEF ≤54%*	2.7 (2.0–3.6)	< 0.0001	2.1 (1.5–3.0)	< 0.001
Age ≥65 yrs	2.8 (2.0–3.8)	< 0.001	2.9 (2.1–4.1)	< 0.001
Diabetes mellitus	2.5 (1.7–3.6)	< 0.001	2.7 (1.8–4.0)	< 0.001
Female	1.6 (1.1–2.3)	0.03	1.5 (1.0–2.2)	0.07
Medical treatment				
Aspirin	0.6 (0.3–1.5)	0.32	0.8 (0.2–3.6)	0.74
Beta-blockers	0.8 (0.4–1.6)	0.71	1.8 (0.6–5.8)	0.32
ACE inhibitor	0.6 (0.3–1.0)	0.06	0.5 (0.2–1.1)	0.09
Statins	0.7 (0.4–1.2)	0.24	0.8 (0.4–1.7)	0.64

*Variables characterizing infarction characteristics (initial perfusion defect, peak creatine kinase, and LVEF) were dichotomized at their median.
ACE = angiotensin-converting enzyme; LVEF = left ventricular ejection fraction.

DISCUSSION

The main finding of our study is that in patients undergoing mechanical reperfusion therapy for acute MI, myocardial salvage as assessed by ^{99m}Tc sestamibi scintigraphy has significant impact on cardiac autonomic function. In our population, patients with high salvage index were more likely to have higher and thus more normal values of DC and TS compared with patients with low salvage index. Patients with low salvage index (<30%) had an almost threefold risk of having either DC or TS abnormal compared with patients who had high salvage index (≥60%), a risk that persisted even after adjustment for initial perfusion defect, maximum creatine kinase level, LVEF, age, sex, presence of diabetes mellitus, and medical therapy. However, salvage index had almost no impact on prognosis if patients already had autonomic dysfunction. When DC and TS were abnormal, patients with low and high salvage index had practically identical poor prognosis. In other words, in this population, myocardial salvage primarily affected the prevalence of autonomic dysfunction but not its prognostic value. Recovery of autonomic dysfunction after MI might, therefore, be an independent mechanism by which patients benefit from reperfusion therapy.

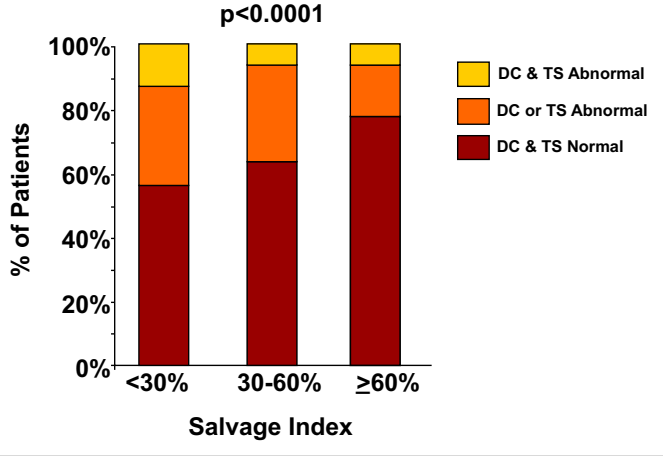

Figure 3. Influence of Myocardial Salvage on Prevalence of Autonomic Dysfunction

Prevalence of autonomic dysfunction in patients with low, medium, and high salvage index. Diagnosis of autonomic dysfunction was based on findings of abnormal deceleration capacity (DC) and/or turbulence slope (TS). **Yellow areas** indicate DC and TS abnormal; **orange areas** indicate DC or TS abnormal; **brown areas** indicate DC and TS normal.

Myocardial salvage was assessed by repeated ^{99m}Tc sestamibi scintigraphy, which is 1 of the most established tools for infarct size measurement (6). Myocardial salvage is correlated with TIMI flow grade of the infarct artery (20), ST-segment resolution (21), and LV systolic function (9). In several randomized trials, myocardial salvage has been shown to be a sensitive tool for the evaluation of the efficacy of interventional and thrombolytic reperfusion strategies (7,8,22).

Autonomic dysfunction, as assessed by HRT and DC, has been shown to be a powerful predictor of death after acute MI independently from reduced LVEF (11–15). Both HRT and DC quantify different aspects of autonomic function: HRT quantifies the physiological response of the sinus node to the transient drop of arterial blood pressure induced by spontaneous VPCs and is linked to baroreflex; in contrast, DC is an integral measure of all periodic deceleration-related oscillations of heart rate observed over 24 h and is presumed to

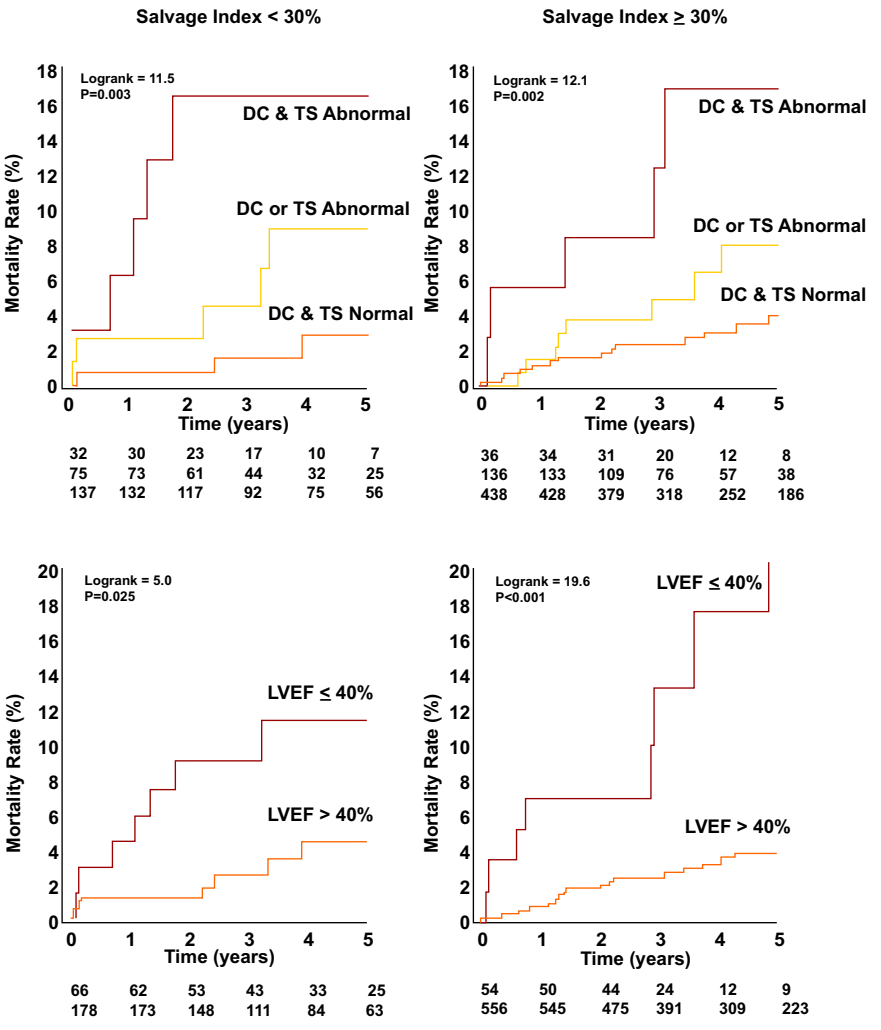

Figure 4. Prognostic Value of Autonomic Dysfunction and LVEF in Salvage Groups

Kaplan-Meier curves of all-cause mortality for patients with low **(left panels)** and medium or high **(right panels)** myocardial salvage stratified by presence or absence of autonomic dysfunction **(upper panels)** and left ventricular dysfunction **(lower panels)**. Patient groups with medium and high salvage index (30% to 60% and ≥60%) were merged because of the low number of end points in these groups. The number of patients of the individual groups involved in the analyses at 0, 1, 2, 3, 4, and 5 years are shown under the graphs. The top, middle, and bottom rows correspond to the upper, middle, and bottom Kaplan-Meier curves, respectively. DC = deceleration capacity; LVEF = left ventricular ejection fraction; TS = turbulence slope.

characterize the tonic predominantly vagal component of autonomic regulation (16). Recently, it has been demonstrated in 2,343 survivors of acute MI that the combination of abnormal DC and HRT identifies patients at very high risk for subsequent death (23). In the present study, we primarily investigated DC and TS, but significant associations with salvage index were also detected for standard measures of HRV. In our patients, low salvage index was also an independent predictor of autonomic dysfunction when defined by other markers of heart rate variability such as low SDNN.

Previous studies already indicated that autonomic dysfunction after acute MI is related to the success of acute therapy. The first evidence came from a subanalysis of the ATRAMI (Autonomic Tone and Reflexes After Myocardial Infarction) trial (4) in which restoration of antegrade flow of the infarct-related artery was associated with preserved baroreflex sensitivity (10). More recently, it was shown in a series of 126 survivors of acute MI in whom serial Holter monitoring had been performed before, during, and after PCI that HRT only recovered when TIMI flow grade 3 was achieved (24). Although restoration of epicardial flow as assessed by TIMI flow should not be equated with restoration of intramyocardial perfusion and salvage of jeopardized myocardium, these findings

Table 4. Multivariable Analysis for Prediction of 5-Year Mortality

Variable	Relative Risk	p Value
Autonomic dysfunction		
TS or DC abnormal	1.9 (0.9–4.0)	0.098
TS and DC abnormal	4.3 (1.8–10.0)	0.001
LVEF ≤40%	3.1 (1.5–6.4)	0.002
Salvage index, %		
<30	0.6 (0.3–1.4)	0.26
30–60	0.6 (0.3–1.3)	0.18

DC = deceleration capacity; LVEF = left ventricular ejection fraction; TS = turbulence slope.

are in agreement with the results of our study. At present, the mechanisms linking successful reperfusion to autonomic function remain speculative. The most likely explanation might be that mechanisms responsible for the initial autonomic impairment after acute MI are counteracted by successful myocardial reperfusion because of hemodynamic improvement, reduction of sympathetic hyperactivity, and suppressed release of neurohumoral factors (24–27).

The limitations of our study have also to be recognized. First, patients older than 75 years were not enrolled. It is known that autonomic function declines with increasing age, and thus, our findings should not be extrapolated to older patients. Second, our study included only patients with sinus rhythm. Therefore, the results cannot be transferred to other patients. Third, the design of our study did not allow for serial assessments of autonomic function to intraindividually detect changes associated with therapy (24). Further, in the present study, 254 (29.7%) patients had no VPCs on the Holter recordings. In line with previous studies, these patients were classified as having normal TS (12,17). However, we also performed separate analyses including only patients with VPCs on Holter and obtained practically the same results. Autonomic function was assessed within the second week after MI. We are unable to comment on the reproducibility of our findings with autonomic function assessed earlier or later after MI. In previous studies, assessment of autonomic markers within the second week after MI proved to be effective in terms of risk prediction (12), which makes our approach relevant for the investigation of the influence of salvage index. The event rate in our population is very low. Therefore, it is difficult to analyze the incremental prognostic value of autonomic dysfunction in relation to LVEF and salvage index in a subgroup analysis. Finally, the process of recovery of the myocardium after MI is a dynamic process that is substantial during the first week after reperfusion. However, there is also a late recovery during the subsequent 6 to 8 months after reperfusion, and late imaging might have provided more accurate measurements of infarct size (28). Nevertheless, virtually all clinical trials that included single-photon emission computed tomography sestamibi infarct size measurements as end points used the time frame between 7 and 14 days after reperfusion to quantify the final infarct (29).

CONCLUSIONS

Despite these limitations, our study provides evidence that autonomic function is linked to myocardial salvage. Thus, "autonomic salvage" might constitute a previously unknown beneficial effect of mechanical reperfusion therapy for acute MI. In this sense, our findings seem to provide additional explanation for the favorable outcome of patients undergoing rigorous reperfusion therapy for acute MI.

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